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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/562,615	07/27/2006	Myung-Hwa Kim	428.1145	6138

20311 7590 06/29/2010

LUCAS & MERCANTI, LLP
475 PARK AVENUE SOUTH
15TH FLOOR
NEW YORK, NY 10016

EXAMINER	
SZNAIDMAN, MARCOS L	

ART UNIT	PAPER NUMBER
1612	

NOTIFICATION DATE	DELIVERY MODE
06/29/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

info@lmiplaw.com

Office Action Summary	Application No.	Applicant(s)	
	10/562,615	KIM ET AL.	
	Examiner	Art Unit	
	MARCOS SZNAIDMAN	1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 May 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *12-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *17,20 and 21* is/are allowed.

6)☒ Claim(s) *12-14,16,18 and 19* is/are rejected.

7)☒ Claim(s) *15* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This office action is in response to applicant's reply filed on May 6, 2010.

Status of Claims

Amendment of claim 12 is acknowledged.

Claims 12-21 are currently pending and are the subject of this office action.

Claims 12-21 are presently under examination.

The examination was expanded to the entire genus encompassed by Formula I which is free of prior art.

Priority

The present application is a 371 of PCT/KR04/01518 filed on 06/23/2004, and claims priority to foreign Application: REPUBLIC OF KOREA 10-2003-00415467 filed on 06/25/2003.

Rejections and/or Objections and Response to Arguments

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated (Maintained Rejections and/or Objections) or newly applied (New Rejections and/or Objections, Necessitated by Amendment or New Rejections and/or Objections not Necessitated by Amendment). They constitute the complete set presently being applied to the instant application.

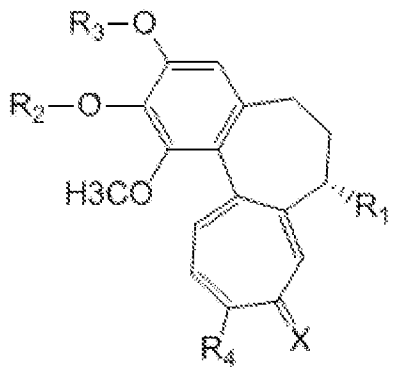
Claim Rejections - 35 USC § 112 (New Rejection not Necessitated by Amendment)

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 12-14, 16 and 18-19 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

Claims 12-14, 16 and 18-19 recite a compound or a pharmaceutical composition comprising a compound of formula I:



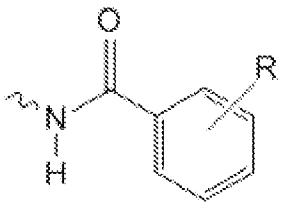
Formula I

M.P.E.P. #2163 states: "An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention….one must define a compound by 'whatever characteristics sufficiently distinguish it'. A lack of adequate written description issue also arises if the knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the product claimed from the disclosed process".

A description of a chemical genus will usually comprise a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the members of the genus, which features constitute substantial portion of the genus. See *Univ. of California vs. Eli Lilly*, 43 USPQ 2d 1398, 1406 (Fed. Cir. 1997). This is analogous to enablement of a genus under section 112 first, by showing enablement of a representative number of species within the genus. A chemical genus can be adequately described if the disclosure presents a sufficient number of

representative species that encompass the genus. If the genus has a substantial variance, the disclosure must describe a sufficient number of species to reflect the variation within that genus.

Applicant has failed to show that he was in possession of all the diverse compounds encompassed by de general structure of Formula I above. Applicant discloses 44 examples of specific structures on pages 44-136 of the specification. These 44 compounds show a very narrow set of substituents at the R1 position which include: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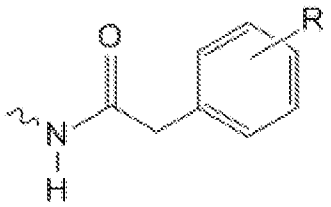
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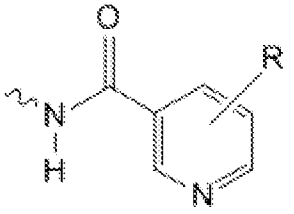
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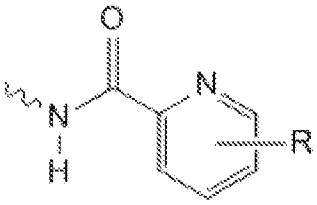
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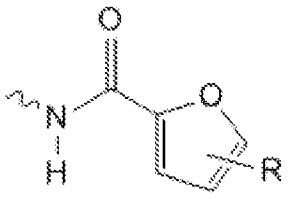
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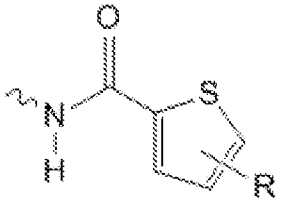
O
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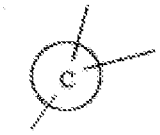
This small set of compounds can not be viewed as being reasonably representative of the genus in its claimed scope because no readily apparent combination of identifying characteristics is provided, other than the disclosure of those specific species as examples of the claimed genus.

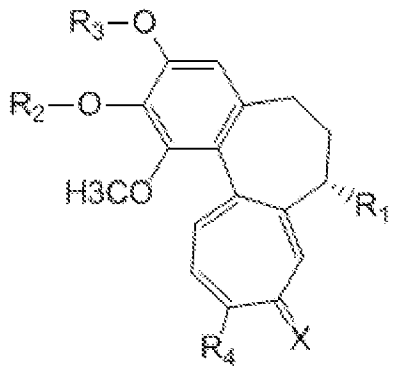
In order to bring the claims in compliance with what is disclosed, it is suggested that applicant provides a more specific and narrower definition of the R1 substituents by eliminating from the claims the compounds wherein B1 is d), e), f), g) h), i), and j) for which there are absolutely no examples; by narrowing down the term heterocycle corresponding to  to the heterocycles disclosed in claim 15; and by narrowing down the definition of T1 to –NHCO-.

Claim Rejections - 35 USC § 112 (New Rejection <u>not</u> Necessitated by Amendment).

Claims 12-14, 16 and 18-19 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the compounds listed in claim 17 does not reasonably provide enablement for the remaining compounds of formula I in claim 1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. <u>This is a scope of enablement rejection</u>.

1. <u>The nature of the invention</u>

Claims 12-14, 16 and 18-19 recite a compound or a pharmaceutical composition comprising a compound of formula I:



Formula I

2. The relative skill of those in the art

The relative skill of those in the art is high, generally that of an M.D. or Ph.D. The artisan using Applicant's invention would generally be a physician with a M.D. degree and several years of experience.

3. The state and predictability of the art

Since the compounds of structure I of claim 1 are novel there is no synthetic procedure for these particular compounds in the prior art.

It is well know in the prior art that organic synthesis is still an experimental science. Even though the knowledge of organic synthesis and the arsenal of chemical reactions have exploded in the last decades, there is still a high degree of unpredictability in organic synthesis. See for example Dorwald F. A. (Side reactions in

organic synthesis, 2005, Wiley, VCH, Weinheim, pg. IX of Preface) where it says: " Most non-chemists would probably be horrified if they were to learn how many attempted synthesis fail, and how inefficient research chemists are. The ratio of successful to unsuccessful chemical experiments in a normal research laboratory is far below unity, and synthetic research chemists, in the same way as most scientists, spend most of their time working on what went wrong, and why. He later states: "The final synthesis usually looks like quite different from that originally planned, because of unexpected difficulties encountered in the initially chosen synthetic sequence. Only the seasoned practitioner who has experienced for himself the many failures and frustrations which the development (sometimes even repetition) of a synthesis usually implies will be able to appraise such work". And finally: "Chemists tend not to publish negative results, because these are, as opposed to positive results, never definitive (and far too copious)."

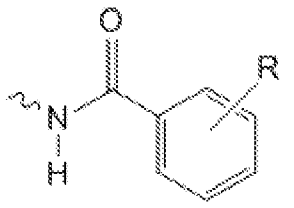
It is also well known that the biological properties highly depend on the core structure and the substituents of the core structure. The more diverse are the substituent, the less likely is that they are going to show similar properties in a biological assay or similar effectiveness in treating a specific disease.

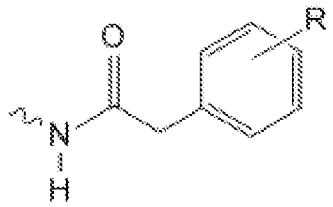
4. The breadth of the claims

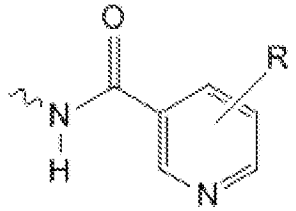
Claims 12-14, 16 and 18-19 are very broad in terms of the number of compounds claimed.

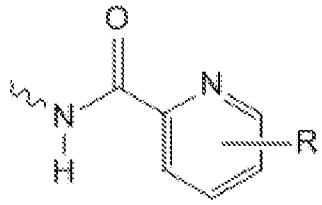
5. The amount of direction or guidance provided and the presence or absence of working examples

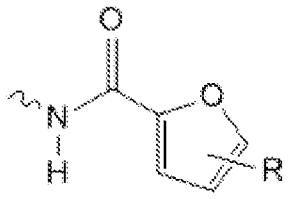
Applicant provides general synthetic schemes (see pages 44-136 of the specification) for 44 compounds. However, even though Applicant claims an extensive and diverse set of substituents for R1, the actual compounds disclosed (44 examples) show a very narrow set of R1 substituents:

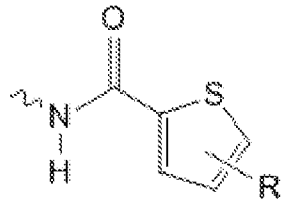












6. The quantity of experimentation necessary

As discussed above (see: 3. the state and predictability of the art), small changes in the structure of one of the reagents could cause a completely different synthetic outcome (i.e. different products, lower yields or no reaction at all). Also, small changes in the substituents of the core structure can cause dramatic changes in biological properties. Based on this, and since applicant provides synthetic and biological data for a small and not very diverse set of compounds (see: 5. The amount of direction or guidance and the presence or absence of working examples above) it is expected that some, if not most of the R1 substituents recited in claim 1 (except for those specifically listed in claim 17) will not provide the desired synthetic outcome outlined by applicant in pages 44-136 of the specification, and also will not posses the same biological properties on tumor growth as shown by most of the 44 compounds disclosed.

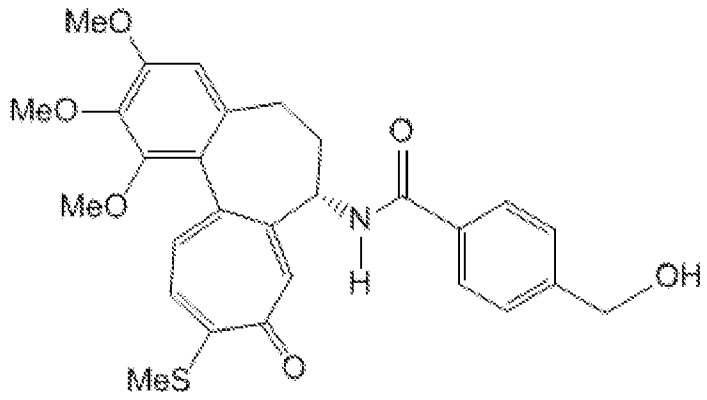
So, determining how to make a particular compound, wherein the compound has a substituent R1 which is not included in claim 17 (or pages 44-136 of the specification), would require testing new synthetic pathways for the different compounds. This is undue experimentation given the limited guidance and direction provided by Applicants.

Accordingly, the inventions of claims 12-14, 16 and 18-19 do not comply with the scope of enablement requirement of 35 U.S.C 112, first paragraph, since to practice the claimed invention a person of ordinary skill in the art would have to engage in undue experimentation with no assurance of success.

Withdrawn Rejections and/or Objections

Claims rejected under 35 USC 102 (b)

Applicant's arguments have been fully considered and are persuasive. The expanded species: 4-(hydroxymethyl(-N-[(7S)-5,6,7,9-tetrahydro-1,2,3-trimethoxy-10-(methylthio)-9-oxobenzo[a]heptalen-7-yl]-benzamide (CAS# 205805-07-8):



was not encompassed by the general structures of formula I.

Rejection under 35 USC 102(b) is withdrawn.

Allowable Subject Matter

Claims 17 and 20-21 are allowed as presently advised.

Claim 15 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

Claims 17 and 20-21 are allowed.

Claim 15 is objected.

Claims 12-14, 16, and 18-19 are rejected.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MARCOS SZNAIDMAN whose telephone number is (571)270-3498. The examiner can normally be reached on Monday through Thursday 8 AM to 6 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick F. Krass can be reached on 571-272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/MARCOS SZNAIDMAN/
June 19, 2010.